

OIPE

RAW SEQUENCE LISTING

DATE: 09/10/2001

PATENT APPLICATION: US/09/689,430

TIME: 09:26:12

Input Set : A:\Seqlist.txt

Output Set: N:\CRF3\09102001\I689430.raw

ENTERED

4 <110> APPLICANT: Walsh, Christopher
 5 Chao, Hengjun
 6 Burstein, Haim
 7 Lynch, Carmel
 8 Stepan, Tony
 9 Munson, Keith

11 <120> TITLE OF INVENTION: Adeno-Associated Virus Vectors Encoding Factor VIII and
 12 Methods of Using the Same

14 <130> FILE REFERENCE: 35052/204375

16 <140> CURRENT APPLICATION NUMBER: US 09/689,430

C--> 17 <141> CURRENT FILING DATE: 2001-08-22

19 <150> PRIOR APPLICATION NUMBER: 60/158,780

20 <151> PRIOR FILING DATE: 1999-10-12

22 <160> NUMBER OF SEQ ID NOS: 5

24 <170> SOFTWARE: FastSEQ for Windows Version 4.0

26 <210> SEQ ID NO: 1

27 <211> LENGTH: 7944

28 <212> TYPE: DNA

29 <213> ORGANISM: Artificial Sequence

31 <220> FEATURE:

32 <223> OTHER INFORMATION: Plasmid pDLZ6 encoding Homo sapiens BDD FVIII

34 <221> NAME/KEY: CDS

35 <222> LOCATION: (420)...(4835)

37 <400> SEQUENCE: 1

38 tggccaactcc ctctctgcgc gctcgtctgc tcactgaggc cgggcgacca aaggtcgccc 60
 39 gacgcccggg ctttgcccg ggcgcctcag tgagcgagcg agcgcgcaga gagggagtgg 120
 40 ccaactccat cactaggggt tcctcagatc tctttctaag taaacagtac atgaaccttt 180
 41 accccgttgc tcggcaacgg cctgggtctgt gccaaagtgtt tgctgacgca acccccactg 240
 42 gctgggggctt ggccataggc catcagcgca tgcggatctc agtgtgggtt tgcaagagga 300
 43 agcaaaaagc ctctccaccc aggcctggaa tgtttccacc caatgtcgag cagtgtgggt 360
 44 ttgcaagagg aagcaaaaag cctctccacc caggcctgga ctcgagagct tcgaccacc 419
 45 atg caa ata gag ctc tcc acc tgc ttc ttt ctg tgc ctt ttg cga ttc 467
 46 Met Gln Ile Glu Leu Ser Thr Cys Phe Phe Leu Cys Leu Leu Arg Phe
 47 1 5 10 15
 49 tgc ttt agt gcc acc aga aga tac tac ctg ggt gca gtg gaa ctg tca 515
 50 Cys Phe Ser Ala Thr Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
 51 20 25 30
 53 tgg gac tat atg caa agt gat ctc ggt gag ctg cct gtg gac gca aga 563
 54 Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro Val Asp Ala Arg
 55 35 40 45
 57 ttt cct cct aga gtg cca aaa tct ttt cca ttc aac acc tca gtc gtg 611
 58 Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn Thr Ser Val Val
 59 50 55 60
 61 tac aaa aag act ctg ttt gta gaa ttc acg gtt cac ctt ttc aac atc 659
 62 Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Val His Leu Phe Asn Ile
 63 65 70 75 80
 65 gct aag cca agg cca ccc tgg atg ggt ctg cta ggt cct acc atc cag 707

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66 Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln
67                               85                               90                               95
69 gct gag gtt tat gat aca gtg gtc att aca ctt aag aac atg gct tcc 755
70 Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser
71                               100                               105                               110
73 cat cct gtc agt ctt cat gct gtt ggt gta tcc tac tgg aaa gct tct 803
74 His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser
75                               115                               120                               125
77 gag gga gct gaa tat gat gat cag acc agt caa agg gag aaa gaa gat 851
78 Glu Gly Ala Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp
79                               130                               135                               140
81 gat aaa gtc ttc cct ggt gga agc cat aca tat gtc tgg cag gtc ctg 899
82 Asp Lys Val Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu
83 145                               150                               155                               160
85 aaa gag aat ggt cca atg gcc tct gac cca ctg tgc ctt acc tac tca 947
86 Lys Glu Asn Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser
87                               165                               170                               175
89 tat ctt tct cat gtg gac ctg gta aaa gac ttg aat tca ggc ctc att 995
90 Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile
91                               180                               185                               190
93 gga gcc cta cta gta tgt aga gaa ggg agt ctg gcc aag gaa aag aca 1043
94 Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr
95                               195                               200                               205
97 cag acc ttg cac aaa ttt ata cta ctt ttt gct gta ttt gat gaa ggg 1091
98 Gln Thr Leu His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly
99                               210                               215                               220
101 aaa agt tgg cac tca gaa aca aag aac tcc ttg atg cag gat agg gat 1139
102 Lys Ser Trp His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp
103 225                               230                               235                               240
105 gct gca tct gct cgg gcc tgg cct aaa atg cac aca gtc aat ggt tat 1187
106 Ala Ala Ser Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr
107                               245                               250                               255
109 gta aac agg tct ctg cca ggt ctg att gga tgc cac agg aaa tca gtc 1235
110 Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val
111                               260                               265                               270
113 tat tgg cat gtg att gga atg ggc acc act cct gaa gtg cac tca ata 1283
114 Tyr Trp His Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile
115                               275                               280                               285
117 ttc ctc gaa ggt cac aca ttt ctt gtg agg aac cat cgc cag gcg tcc 1331
118 Phe Leu Glu Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser
119                               290                               295                               300
121 ttg gaa atc tcg cca ata act ttc ctt act gct caa aca ctc ttg atg 1379
122 Leu Glu Ile Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met
123 305                               310                               315                               320
125 gac ctt gga cag ttt cta ctg ttt tgt cat atc tct tcc cac caa cat 1427
126 Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His
127                               325                               330                               335
129 gat ggc atg gaa gct tat gtc aaa gta gac agc tgt cca gag gaa ccc 1475
130 Asp Gly Met Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro

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131		340		345		350		
133	caa cta cga atg aaa aat aat gaa gaa gcg gaa gac tat gat gat gat							1523
134	Gln Leu Arg Met Lys Asn Asn Glu Glu Ala Glu Asp Tyr Asp Asp Asp							
135		355		360		365		
137	ctt act gat tct gaa atg gat gtg gtc agg ttt gat gat gac aac tct							1571
138	Leu Thr Asp Ser Glu Met Asp Val Val Arg Phe Asp Asp Asp Asn Ser							
139		370		375		380		
141	cct tcc ttt atc caa att cgc tca gtt gcc aag aag cat cct aaa act							1619
142	Pro Ser Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr							
143	385		390		395			400
145	tggt gta cat tac att gct gct gaa gag gag gac tgg gac tat gct ccc							1667
146	Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro							
147		405		410		415		
149	tta gtc ctc gcc ccc gat gac aga agt tat aaa agt caa tat ttg aac							1715
150	Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn							
151		420		425		430		
153	aat ggc cct cag cgg att ggt agg aag tac aaa aaa gtc cga ttt atg							1763
154	Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met							
155		435		440		445		
157	gca tac aca gat gaa acc ttt aag act cgt gaa gct att cag cat gaa							1811
158	Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu							
159		450		455		460		
161	tca gga atc ttg gga cct tta ctt tat ggg gaa gtt gga gac aca ctg							1859
162	Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu							
163	465		470		475			480
165	ttg att ata ttt aag aat caa gca agc aga cca tat aac atc tac cct							1907
166	Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro							
167		485		490		495		
169	cac gga atc act gat gtc cgt cct ttg tat tca agg aga tta cca aaa							1955
170	His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys							
171		500		505		510		
173	ggt gta aaa cat ttg aag gat ttt cca att ctg cca gga gaa ata ttc							2003
174	Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe							
175		515		520		525		
177	aaa tat aaa tgg aca gtg act gta gaa gat ggg cca act aaa tca gat							2051
178	Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp							
179		530		535		540		
181	cct cgg tgc ctg acc cgc tat tac tct agt ttc gtt aat atg gag aga							2099
182	Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg							
183	545		550		555			560
185	gat cta gct tca gga ctc att ggc cct ctc ctc atc tgc tac aaa gaa							2147
186	Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu							
187		565		570		575		
189	tct gta gat caa aga gga aac cag ata atg tca gac aag agg aat gtc							2195
190	Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val							
191		580		585		590		
193	atc ctg ttt tct gta ttt gat gag aac cga agc tgg tac ctc aca gag							2243
194	Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu							
195		595		600		605		

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197 aat ata caa cgc ttt ctc ccc aat cca gct gga gtg cag ctt gag gat 2291
198 Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp
199 610 615 620
201 cca gag ttc caa gcc tcc aac atc atg cac agc atc aat ggc tat gtt 2339
202 Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val
203 625 630 635 640
205 ttt gat agt ttg cag ttg tca gtt tgt ttg cat gag gtg gca tac tgg 2387
206 Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp
207 645 650 655
209 tac att cta agc att gga gca cag act gac ttc ctt tct gtc ttc ttc 2435
210 Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe
211 660 665 670
213 tct gga tat acc ttc aaa cac aaa atg gtc tat gaa gac aca ctc acc 2483
214 Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr
215 675 680 685
217 cta ttc cca ttc tca gga gaa act gtc ttc atg tcg atg gaa aac cca 2531
218 Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro
219 690 695 700
221 ggt cta tgg att ctg ggg tgc cac aac tca gac ttt cgg aac aga ggc 2579
222 Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly
223 705 710 715 720
225 atg acc gcc tta ctg aag gtt tct agt tgt gac aag aac act ggt gat 2627
226 Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp
227 725 730 735
229 tat tac gag gac agt tat gaa gat att tca gca tac ttg ctg agt aaa 2675
230 Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys
231 740 745 750
233 aac aat gcc att gaa cca aga agc ttc tcc cag aat tca aga cac cct 2723
234 Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Ser Arg His Pro
235 755 760 765
237 agc act agg caa aag caa ttt aat gcc acc cca cca gtc ttg aaa cgc 2771
238 Ser Thr Arg Gln Lys Gln Phe Asn Ala Thr Pro Pro Val Leu Lys Arg
239 770 775 780
241 cat caa cgg gaa ata act cgt act act ctt cag tca gat caa gag gaa 2819
242 His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser Asp Gln Glu Glu
243 785 790 795 800
245 att gac tat gat gat acc ata tca gtt gaa atg aag aag gaa gat ttt 2867
246 Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys Lys Glu Asp Phe
247 805 810 815
249 gac att tat gat gag gat gaa aat cag agc ccc cgc agc ttt caa aag 2915
250 Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg Ser Phe Gln Lys
251 820 825 830
253 aaa aca cga cac tat ttt att gct gca gtg gag agg ctc tgg gat tat 2963
254 Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg Leu Trp Asp Tyr
255 835 840 845
257 ggg atg agt agc tcc cca cat gtt cta aga aac agg gct cag agt ggc 3011
258 Gly Met Ser Ser Ser Pro His Val Leu Arg Asn Arg Ala Gln Ser Gly
259 850 855 860
261 agt gtc cct cag ttc aag aaa gtt gtt ttc cag gaa ttt act gat ggc 3059

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262 Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu Phe Thr Asp Gly
263 865 870 875 880
265 tcc ttt act cag ccc tta tac cgt gga gaa cta aat gaa cat ttg gga 3107
266 Ser Phe Thr Gln Pro Leu Tyr Arg Gly Glu Leu Asn Glu His Leu Gly
267 885 890 895
269 ctc ctg ggg cca tat ata aga gca gaa gtt gaa gat aat atc atg gta 3155
270 Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val
271 900 905 910
273 act ttc aga aat cag gcc tct cgt ccc tat tcc ttc tat tct agc ctt 3203
274 Thr Phe Arg Asn Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu
275 915 920 925
277 att tct tat gag gaa gat cag agg caa gga gca gaa cct aga aaa aac 3251
278 Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg Lys Asn
279 930 935 940
281 ttt gtc aag cct aat gaa acc aaa act tac ttt tgg aaa gtg caa cat 3299
282 Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val Gln His
283 945 950 955 960
285 cat atg gca ccc act aaa gat gag ttt gac tgc aaa gcc tgg gct tat 3347
286 His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr
287 965 970 975
289 ttc tct gat gtt gac ctg gaa aaa gat gtg cac tca ggc ctg att gga 3395
290 Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly
291 980 985 990
293 ccc ctt ctg gtc tgc cac act aac aca ctg aac cct gct cat ggg aga 3443
294 Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His Gly Arg
295 995 1000 1005
297 caa gtg aca gta cag gaa ttt gct ctg ttt ttc acc atc ttt gat gag 3491
298 Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu
299 1010 1015 1020
301 acc aaa agc tgg tac ttc act gaa aat atg gaa aga aac tgc agg gct 3539
302 Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys Arg Ala
303 1025 1030 1035 1040
305 ccc tgc aat atc cag atg gaa gat ccc act ttt aaa gag aat tat cgc 3587
306 Pro Cys Asn Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn Tyr Arg
307 1045 1050 1055
309 ttc cat gca atc aat ggc tac ata atg gat aca cta cct ggc tta gta 3635
310 Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly Leu Val
311 1060 1065 1070
313 atg gct cag gat caa agg att cga tgg tat ctg ctc agc atg ggc agc 3683
314 Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser
315 1075 1080 1085
317 aat gaa aac atc cat tct att cat ttc agt gga cat gtg ttc act gta 3731
318 Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe Thr Val
319 1090 1095 1100
321 cga aaa aaa gag gag tat aaa atg gca ctg tac aat ctc tat cca ggt 3779
322 Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr Pro Gly
323 1105 1110 1115 1120
325 gtt ttt gag aca gtg gaa atg tta cca tcc aaa gct gga att tgg cgg 3827
326 Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile Trp Arg

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VERIFICATION SUMMARY

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L:17 M:271 C: Current Filing Date differs, Replaced Current Filing Date